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MORPHOLOGICAL INDICATORS OF LIVER TISSUE STATE IN CHOLESTASIS BEFORE AND AFTER DECOMPRESSION

T.K.Dubovaya*, L.G.Proshina, M.D.Kashaeva, A.V.Proshin, K.V.Gavrilova

МОРФОЛОГИЧЕСКИЕ ПОКАЗАТЕЛИ СОСТОЯНИЯ ТКАНИ ПЕЧЕНИ ПРИ ХОЛЕСТАЗАХ ДО И ПОСЛЕ ДЕКОМПРЕССИИ

Т.К.Дубовая*, Л.Г.Прошина, М.Д.Кашаева, А.В.Прошин, К.В.Гаврилова

Новгородский государственный университет имени Ярослава Мудрого
**Российский национальный исследовательский медицинский университет имени Н.И. Пирогова, Москва*

The morphological state of the liver was analyzed in 145 patients with cholestasis of non-neoplastic etiology, who were treated at the Novgorod Regional Clinical Hospital and the Central City Clinical Hospital of Veliky Novgorod. The results of liver biopsy during surgery, as well as puncture liver biopsy 5 days and 3 weeks after decompression operations were studied. There were pronounced structural and functional changes in liver tissue that progressed with increasing duration of occlusion. In cases with prolonged chronic jaundice, after decompression of the bile ducts, sclerotic changes, histiolymphocytic infiltration and proliferating biliary epithelium remain in the portal tracts. The study of puncture and intraoperative biopsies in obstructive jaundice makes it possible to determine the form and severity of cholestasis, which, together with other data, affects the prognosis of the disease and the tactics of surgical treatment. With cholestasis of varying duration, it is necessary to carry out measures as early as possible aimed at correcting violations of liver morphology.

Keywords: needle aspiration and intraoperative biopsy, morphology of the liver, cholestasis of non-tumor etiology, duration of occlusion

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Проведен анализ морфологического состояния печени у 145 больных с холестазами неопухолевой этиологии, находившихся на лечении в НОКБ и ЦГКБ Великого Новгорода. Исследованы результаты биопсии печени во время операции, а также пункционной биопсии печени через 5 дней и через 3 недели после декомпрессионных операций. Выявлены выраженные структурные и функциональные изменения ткани печени, которые прогрессировали с увеличением длительности окклюзии. В случаях с длительной хронической желтухой после декомпрессии желчных протоков в портальных трактах остаются склеротические изменения, гистиолимфоцитарная инфильтрация и пролиферирующий билиарный эпителий. Исследование пункционных и интраоперационных биопсий при механической желтухе позволяет определить форму и тяжесть холестаза, что совместно с другими данными влияет на прогноз заболевания и на тактику оперативного лечения. При холестазах различной длительности необходимо как можно раньше проводить мероприятия, направленные на коррекцию нарушений морфологии печени.

Ключевые слова: пункционная и интраоперационная биопсия, морфология печени, холестазы неопухолевой этиологии, длительность окклюзии

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Introduction

Obstructive jaundice is the most severe complication of many diseases of the hepatopancreatic zone with localization of obstruction in various extrahepatic and intrahepatic ducts. Among the main reasons for the development of obstructive jaundice, one can single out cholelithiasis and choledocholithiasis in 45-55% of cases, tumors of the hepatobiliary region in 35-45% of cases, as well as purulent and sclerosing cholangitis, cicatricial strictures, pancreatitis and pancreatic cysts in 7-10% of cases [1,2]. Moreover, the latter group of diseases is most often the cause of chronic recurrent jaundice. Obstructive jaundice is based on the obstruction of the outflow of bile from the liver into the biliary system. Obstruction of the flow of bile leads to an increase in pressure in the overlying biliary tract. In this case, the bile pigment diffuses through the walls of the dilated bile ducts into hepatocytes, sinusoidal spaces and into the blood [3,4]. Cholestasis with mechanical obstacles in the biliary tract leads to profound disturbances in the structure of hepatocytes, to cholestatic endogenous intoxication. Prolonged obstructive jaundice determines the development of severe violations of all liver functions, which is manifested by liver failure and leads to high mortality [4,5]. Morphological studies of intraoperative liver biopsies in the practice of hepatobiliary surgery is one of the reliable methods in

diagnosing the causes of obstructive jaundice and assessing the prognosis of liver failure, allowing timely and complete treatment [5,6].

The purpose of this study is to study the histological structure of liver tissue in obstructive jaundice of non-neoplastic etiology of various durations before and after decompression operations on the biliary tract.

Research Methods and Materials

In accordance with this goal, intraoperative liver biopsies were studied in 145 patients with obstructive jaundice of non-neoplastic etiology, who were treated at the Novgorod Regional Clinical Hospital and the Central City Clinical Hospital of Veliky Novgorod. In 98 cases, the causes of obstructive jaundice were cholelithiasis and choledocholithiasis, and in 47 cases obstructive jaundice was caused by other causes, including strictures of the extrahepatic bile ducts, sclerosing halangitis and cyst of the head of the pancreas. There were 22.1% of men and 77.9% of women. All patients underwent a blood test with the determination of platelets according to Fonio. The functional state of the liver was assessed by the results of biochemical blood tests.

In the first group of 98 patients, jaundice appeared 2 weeks before hospitalization. Jaundice, as a rule, occurred acutely, after a painful attack in the form of typical colic with pain radiating to the right shoulder blade and arm. There was an increase in temperature to 38 - 39 C. The total bilirubin figures ranged from 90 to 400 μmol/l. Examination in all cases was diagnosed with cholelithiasis, choledocholithiasis. After appropriate preparation, operations were performed laparoscopic cholecystectomy, choledocholithotomy.

In 47 patients of the second group, jaundice was recurrent, periodically occurring for two to three years. The total bilirubin values ranged from 160 to 580 μmol/L. In this group, reconstructive operations on the bile ducts were performed with the imposition of various types of biliodigestive anastomoses.

All patients underwent liver biopsy during surgery, as well as puncture liver biopsy 5 days and 3 weeks after decompression operations. Surgical biopsies, represented by pieces of liver tissue with a diameter of 0.5 cm, puncture biopsies, represented by columns 1.0 cm long with a diameter of 0.1 cm, were fixed in 10% neutral formalin, carried out using a battery in an AT-4 automatic laboratory assistant and poured into paraffin. 20-25 sections were made from each block. Sections were stained for review using the conventional technique with hematoxylin and eosin. To identify collagen fibers and connective tissue, picric acid and acid fuchsin were stained according to the Van Gieson method. In addition, histochemical studies were carried out with Prussian blue to identify iron and hemosiderin according to the Perls method.

Results and Discussion

The studies performed showed that with cholestasis lasting up to 2 weeks, caused by cholelithiasis and choledocholithiasis, the distribution of bilirubin in the central part of the lobule is characteristic, centrilobular cholestasis is noted. With mild jaundice, with total bilirubin numbers less than 100 μmol/l, dusty and fine-grained bilirubin inclusions are found in individual hepatocytes, stellate reticulo endotheliocytes (RRE) and in the bile ducts of the third zone. In other zones of the hepatic lobule, bilirubin inclusions are not observed. The cytoplasm of hepatocytes of the third zone is slightly cloudy, and the cytoplasm of hepatocytes of the second and first zones is of normal structure. The central veins and sinusoids are somewhat collapsed. Portal tracts are of a conventional structure. With moderate jaundice with bilirubin numbers up to 300 μmol/l, centrilobular cholestasis is more pronounced. The number of hepatocytes and stellate reticulo endotheliocytes, in which bilirubin inclusions are determined, increased in comparison with the previous degree of severity, the inclusions look like lumps of various sizes. Individual hepatocytes, completely filled with bilirubin, are identified. In the bile tubules of the third zone, accumulations of bilirubin are detected. In the hepatocytes of the second zone, adjacent to the third, very small, dusty inclusions of bilirubin appear. Hepatocytes of the third zone show manifestations of protein dystrophies, in other parts of the hepatic lobule hepatocytes retain their usual structure. The lumens of the central veins and sinusoids are collapsed. Portal tracts are of a conventional structure. In severe jaundice with total bilirubin values above 300 μmol/l, there is a pronounced cholestasis of the third zone. The majority of hepatocytes and stellate reticulo endotheliocytes are filled with inclusions of bilirubin of various sizes, individual hepatocytes of this zone are completely filled with bile, and in some places are subject to necrosis. The bile ducts of this zone are dilated with the presence of bile stasis and bile blood clots. In hepatocytes and Cooper's cells of the third zone of the hepatic lobule, fine-grained inclusions of bilirubin are visible. There is marked centrilobular cholestasis with the transition to the second zone of the hepatic lobule (Fig. 1). Bile accumulates in the bile ducts. At high levels of bilirubin, necrosis of hepatocytes with insignificant intralobular inflammatory infiltration and bile lakes are determined. In the portal tracts, there is stromal edema, slight proliferation of connective tissue and histiolymphocytic infiltration, as well as proliferation of the biliary epithelium along the edges of the portal tract.

Repeated biopsies of this group of patients 5 days after decompression showed a slight decrease in cholestasis of the third zone of the hepatic lobule. Bilirubin in the third zone is unevenly distributed, areas of hepatocytes and stellate reticulo endotheliocytes filled with coarse-grained bilirubin inclusions and areas where bile pigments are absent are visible. The central veins and sinusoids are dilated, overflowing with erythrocytes. No changes were noted in the portal tracts. 3 weeks after decompression, patients of the first group showed a significant decrease in cholestasis and the level of protein dystrophies in all parts of the hepatic lobule. In intralobular inflammatory infiltrates, a greater number of macrophages appear. The central veins and sinusoids are full-blooded, somewhat dilated, filled with erythrocytes. Portal tracts are of a conventional structure. In the study

of repeated biopsies of patients with total bilirubin values above 200 μmol/l, there is a significant decrease in cholestasis in all parts of the lobule, however, bilirubin deposits in the form of coarse and fine-grained inclusions are visible in hepatocytes and stellate reticulo endotheliocytes of the central zone. In the second zone, dust-like inclusions of bilirubin are visible, in hepatocytes of the first zone, inclusions of bile pigments were not found. In the third zone, among the parenchyma of the hepatic lobule, single, small-focal inflammatory infiltrates are seen, consisting of neutrophilic leukocytes and macrophages. Hepatocytes mainly of the third zone in a state of protein dystrophy, in other parts of the usual structure. Groups of regenerating hepatocytes are found periportally. In the portal tracts, slight growths of connective tissue and histio-lymphocytic infiltration. In the marginal zones of the portal tracts, there is a slight proliferation of the biliary epithelium.

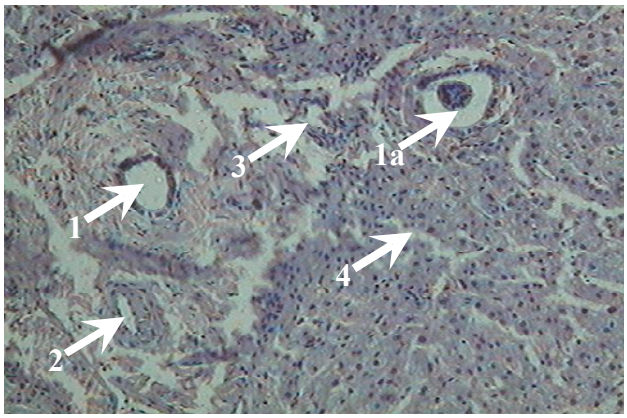

Fig.1. Photo Histogram. Liver tissue. Hematoxylin-eosin staining, enlarged ×150. 1 — bile duct, 2 — hepatic artery, 3 — vein, 4 — dilated sinusoids between trabeculae

A study of patients with long-term cholestasis and chronic reductive jaundice revealed diffuse cholestasis with deposition of bile pigments in hepatocytes and stellate reticulo endotheliocytes in all parts of the hepatic lobule. Moreover, with a longer jaundice, pronounced cholestasis is noted in the first zone of the hepatic lobule. The bile ducts are dilated, filled with bile. In separate tubules, bile clots and microliths are visible. Many hepatocytes filled with bile are lysed or subject to apoptosis with the development of biliary infarctions and perifocal inflammatory infiltrates. Regenerating hepatocytes are visible around the heart attacks and in the first hepatic lobule. Most hepatocytes are with hyaline droplet phenomena. Around the central veins, hepatocytes are subject to necrotic changes. The central veins are dilated, in their walls there is a proliferation of connective tissue, which passes to the adjacent sinusoids, their lumens collapsed, individual sinusoids are dilated, filled with red blood cells. In the portal tracts, extensive growths of connective tissue with abundant histiolymphocytic infiltration far beyond the portal tracts with the formation in some cases of connective tissue interportal septa. In cases with cholangitis, a large number of neutrophilic leukocytes and macrophages appear in the infiltrate, which spread to the walls of the bile ducts and appear in their lumens. In the portal tracts, there is a pronounced proliferation of the bile ducts and biliary epithelium with the formation of false bile ducts (Fig.2,3,4,5,6,7).

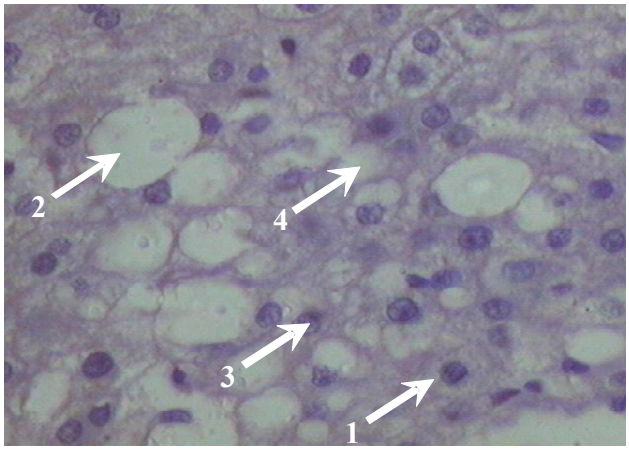

Fig.2. Photo Histogram. Liver tissue. Hematoxylin-eosin staining, enlarged ×600. 1 — protein dystrophy, 2 — dilated bile capillary, 3 — hepatocyte nucleus, 4 — balloon dystrophy of hepatocyte

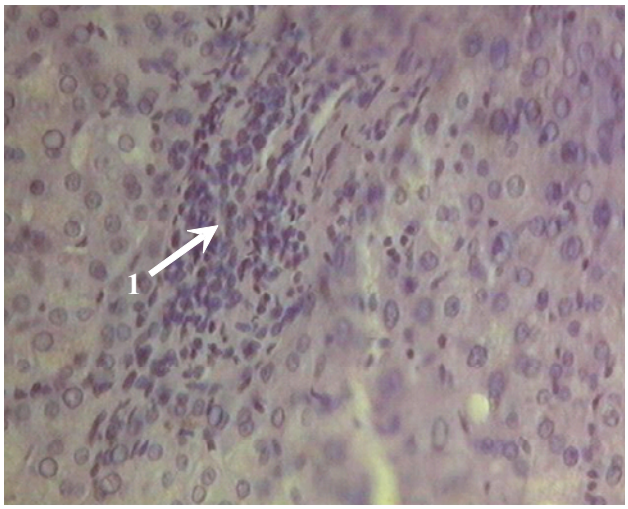

Fig.3. Photo Histogram. Liver tissue. Hematoxylin-eosin staining, enlarged ×300. 1 —lymphoid infiltration of the portal tract with the presence of macrophages, the boundaries of infiltration are indistinct

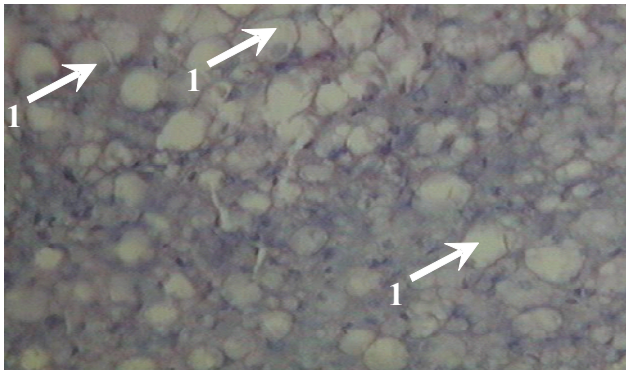

Fig.4. Photo Histogram. Liver tissue. Hematoxylin-eosin staining, enlarged ×300. 1 — balloon dystrophy of hepatocytes is pronounced

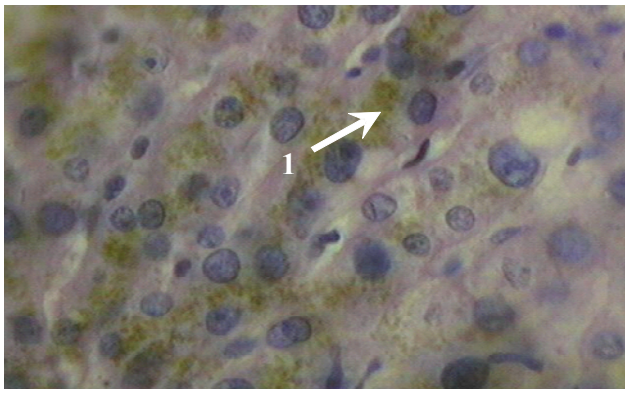

Fig.5. Photo Histogram. Liver tissue. Hematoxylin-eosin staining, enlarged ×600. 1 — accumulation of bile pigments

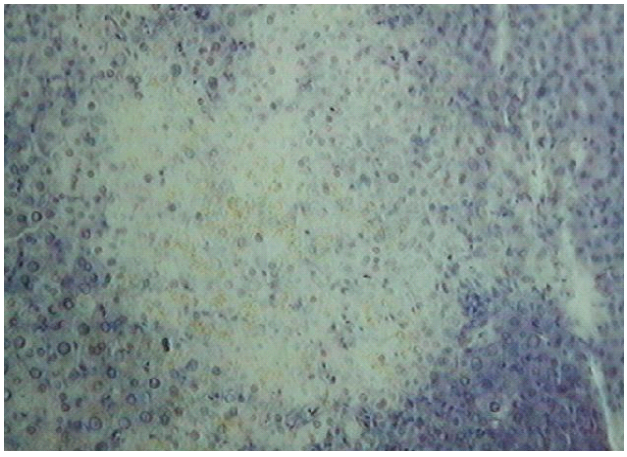

Fig.6. Photo Histogram. Liver tissue. Hematoxylin-eosin staining, enlarged ×150. In the center is hepatocyte necrosis with accumulation of bile pigments. Disorganization of hepatocytes is detected along the periphery

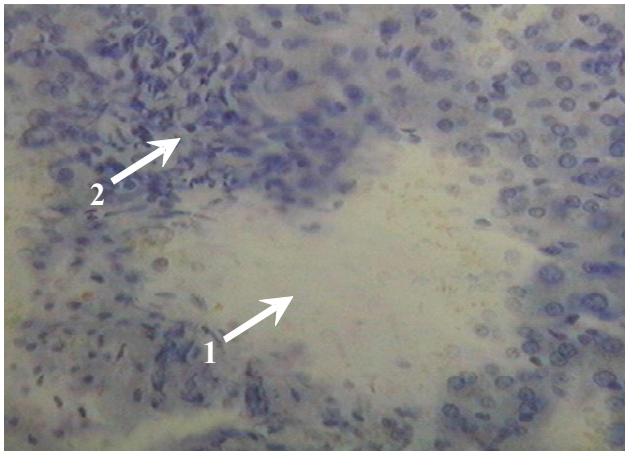

Fig.7. Photo Histogram. Liver tissue. Hematoxylin-eosin staining, enlarged ×300. 1 — focus of necrosis, 2 — focus of lymphoid-cell infiltration

Thus, chronic recurrent jaundice is characterized by diffuse cholestasis with necrosis of hepatocytes, the development of biliary infarctions and the formation of bile lakes. The bile ducts are dilated, with bile stasis, bile clots and microliths in their lumens. In the portal tracts and periportally, there are extensive growths of connective tissue with the development of liver fibrosis. There is an extensive histiolymphocytic infiltration, in cases with cholangitis — with accompanying lymphocytes with neutrophilic leukocytes and macrophages. 5 days after decompression in this group of patients there is a slight decrease in cholestasis in the second zone and practically unchanged amount of bilirubin in the third zone of the hepatic lobule.

The central vein and sinusoids are dilated, overflowing with erythrocytes. The central vein and sinusoids are dilated, overflowing with erythrocytes.

When studying liver biopsies in this group of patients 3 weeks after decompression, there is a decrease in cholestasis in all parts of the hepatic lobule, especially in the first zone; in some cases, deposits of bile pigment in the first zone of the hepatic lobule are not detected. In the second and third zones, bilirubin in hepatocytes and stellate reticulo endotheliocytes is in the form of granules of various sizes. Bile ducts are of normal size, filled with bile. In the cytoplasm of hepatocytes, cirrus dystrophy is determined mainly in the third zone. In most cases, the walls of the central veins and sinusoids are of normal structure, but in some cases, connective tissue of varying degrees of maturity is determined. In different parts of the hepatic lobule, single areas of small focal sclerosis are visible, around which accumulations of fibroblasts and proliferating hepatocytes are visible. In the periportal regions, groups and nodules of regenerating hepatocytes are determined. Liver parenchyma, especially in the third zone, with phenomena of various types of protein dystrophies. The portal tracts are enlarged, represented by growths of connective tissue, which in most cases penetrates beyond the portal fields and connects with the adjacent portal tracts with the formation of liver fibrosis. In the course of the proliferation of connective tissue, extensive accumulations of histiolymphocytic elements are visible. In cases with cholangitis in the portal tracts, in addition to histiolymphocytic infiltration, dense leukocytic infiltration with macrophages is determined, which spreads to the walls of the bile ducts, but no pus is detected in the lumen of the ducts. Periductally determined by the proliferation of the bile ducts and biliary epithelium, which forms the false bile ducts. Thus, in patients with chronic recurrent jaundice 3 weeks after decompression of the bile ducts in liver biopsies, there is a significant decrease in cholestasis in all parts of the hepatic lobule. In the liver parenchyma, the level of intracellular dystrophies decreases, biliary infarctions are organized and regression in individual hepatic lobules of sclerosis in the walls of the central veins and sinusoids occurs. Groups of regenerating hepatocytes are visible mainly in the near-portal regions. The bile ducts take on a normal structure. At the same time, pronounced sclerotic changes remain in the portal tracts and periportal spaces with the formation of liver fibrosis. In the course of the growths of connective tissue, a dense histiolymphocytic infiltration is noted, in cases with cholangitis, neutrophilic leukocytes join the infiltrate. In the portal tracts, there is a pronounced proliferation of the biliary epithelium and bile ducts.

Conclusion

In patients with obstructive jaundice of various etiologies after decompression, there is a decrease in bilirubin, especially of the indirect fraction, a tendency towards a decrease in aspartate aminotransferase and alanine aminotransferase.Histological examination reveals a slight decrease in cholestasis and plethora appears in the vessels of the microvasculature. 3 weeks after decompression, a significant decrease in bilirubin occurs, in cases of short-term occlusions, its restoration to normal values, a decrease in aspartate aminotransferase and alanine aminotransferase is noted. Histological examination reveals a pronounced decrease in cholestasis, and with jaundice lasting up to two weeks, the structure of the liver is practically restored.In cases with prolonged chronic jaundice, sclerotic changes, histiolymphocytic infiltration and proliferating biliary epithelium remain in the portal tracts.

Thus, the study of puncture and intraoperative biopsies in obstructive jaundice makes it possible to determine the form and severity of cholestasis, which, together with other data, affects the prognosis of the disease and the tactics of surgical treatment. In addition, the data of puncture liver biopsies can be one of the histological criteria in determining the indications for the use of hybrid extracorporeal detoxification. Repeated puncture liver biopsies allow monitoring the state of the liver after decompression and determine the effectiveness of the treatment. The absence of any complications in our study indicates the advisability of taking operational and puncture liver biopsies for morphological studies in patients with obstructive jaundice.

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